

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
(Case No. 98,614-D)

In re Application of: )  
 )  
John DeBernardis, et al. )  
 )  
U.S Application No.: 10/017,822 ) Examiner: S. Gucker  
 )  
Application Filing Date: December 12, 2001 ) Group Art Unit: 1647  
 )  
For: Purified Antigen for Alzheimer's Disease, )  
and Methods of Obtaining and Using Same )

**INFORMATION DISCLOSURE STATEMENT**

Mail Stop RCE  
Commissioner of Patents  
P.O. Box 1450  
Alexandria VA 22313-1450

Dear Sir:

This prior art statement is filed under 37 C.F.R. §§1.97-1.98 in compliance with the duty of disclosure set forth in 37 C.F.R. §1.56. Applicants respectfully request that this statement together with the attached Form PTO-1449 and accompany references be placed in the file for the subject application.

In the judgment of the undersigned, the references listed on the attached Form PTO-1449 may be material to the Examiner's consideration of the presently pending claims. However, the references have not been reviewed in sufficient detail to make any other representation and, in particular, no representation is intended as to the relative relevance between references, whether cited in this statement or prior statements. This statement is not a representation that the listed references have effective dates early enough to be "prior art" within the meaning of 35 U.S.C. §102.

1. H. Paul Vooheis, U.S. Patent 5,492,812, issued February 20, 1996.
2. G. Hossein , WO 96 20218 A, issued July 4, 1996
3. M. Gesellschaft, EP 0 909 814 A, issued April 21, 1999.
4. Foley et al., (1988), "Evidence for the presence of antibodies to cholinergic neurons in the serum of patients with Alzheimer's disease", *Journal of Neurology*, Vol. 235, pp. 466-471.
5. Gaskin, "Human Antibodies to Alzheimer's Disease and Normal Neural Elements", *Antibodies to Alzheimer's Disease*, pp 137-145.
6. Gaskin et al., (January 1987), "Autoantibodies To Neurofibrillary Tangles and Brain Tissue in Alzheimer's Disease: Establishment of Epstein-Barr Virus-transformed Antibody-producing Cell Lines", *J. Exp. Med.*, Vol. 165, pp. 245-250.
7. Lopez et al., (August 1992), "Serum Autoantibodies in Patients With Alzheimer's Disease and Vascular Dementia and in Nondemented Control Subjects", *Stroke*, Vol. 23, No. 8, pp. 1078-1083.
8. McRae et al., (August 1993), "Cerebrospinal fluid microglial antibodies: potential diagnostic markers for immune mechanisms in Alzheimer's disease", *Behavioural Brain Research*, Vol. 57, pp. 225-234.
9. Mecocci et al., (1993), "Antihistone and Anti-dsDNA Autoantibodies in Alzheimer's Disease and Vascular Dementia", *Society of Biological Psychiatry*, Vol. 33, pp. 380-385.
10. Mecocci et al., (1995), "Serum anti-GFAP and anti-S100 autoantibodies in brain aging, Alzheimer's disease and vascular dementia", *Journal of Neuroimmunology*, Vol. 57, pp. 165-170.
11. Singh et al., (1992), "Immunoblot detection of antibodies to myelin basic protein in Alzheimer's disease patients", *Neuroscience Letters*, Vol. 147, pp. 25-28.
12. Singh et al., (1986), "Detection of Brain Autoantibodies in the serum of patients with Alzheimer's disease but not Down's Syndrome", *Immunology Letters*, Vol. 12, pp. 277-280.
13. Tanaka et al., (1989), "Enzyme-linked immunosorbent assay for human autoantibody to glial fibrillary acidic protein: higher titer of the antibody is detected in serum of patients with Alzheimer's disease", *Acta Neurol. Scand.*,

Vol. 80, pp. 554-560.

14. Tchernakov et al., (1992), "Alzheimer's disease and Down's syndrome antibodies bind to the heavy neurofilament protein of cholinergic neurons", *Immunological Factors in Alzheimer's Disease*, pp. 670-675.
15. Schott et al. (January 31, 1996), "Autoantibody reactivity in serum of patients with Alzheimer's disease and other age related dementia", *Psychiatry Res.*, Vol. 50, No. 3, pp. 251-54. (Abstract).
16. Lopez et al., (November 1991), "Serum auto-antibodies in Alzheimer's disease" *Acta Neural Scand*, Vol. 84, No. 5, pp. 441-44. (Abstract).
17. Ounanian et al., (1990), "Antibodies to viral antigens, xenoantigens and autoantigens in Alzheimer's disease". *J Clin Lab Anal*, Vol. 4, No. 5, pp. 367-75. (Abstract).
18. Loeffler et al, (February 1997), "Immunocytochemical detection of anti-hippocampal antibodies in Alzheimer's disease and normal cerebrospinal fluid", *Neurochem Res.*, Vol. 22, No. 2 pp. 209-14. (Abstract).
19. McRae et al., (May-August 1996), "Microglial Cerebrospinal fluid antibodies. Significance for Alzheimer disease", *Mol. Chem. Neuropathol*, Vol. 28, No. 1-3, pp. 89-95. (Abstract).
20. Dahlstrom et al., (August-December 1994), "Alzheimer's disease cerebrospinal fluid antibodies display selectivity for Microglia. Investigations with cell cultures and human cortical biopsies" *Mol Neurobiol*, Vol. 9, No. 1-3, pp. 41-54. (Abstract).
21. Dahlstrom et al., (1990), "Investigations on auto-antibodies in Alzheimer's and Parkinson's disease, using defined neuronal cultures" *J Neural Transm Suppl.*, Vol. 29, 195-206. (Abstract).
22. Sugiura et al., (January 1989), "Detection of anti-cerebral autoantibodies in schizophrenia and Alzheimer's disease" *J Clin lab Immunol*, Vol. 28, No. 1, pp. 1-3. (Abstract).
23. Bahmanyar et al., (October 1983), "Serum antibodies to neurofilament antigens in patients with neurological and other diseases and in healthy controls", *J Neuroimmunol*, Vol. 5, No. 2, pp. 191-196. (Abstract).
24. Genovesi et al., (March 1996), "Relationship between autoimmune thyroid disease and Alzheimer's disease", *Panminerva Med.*, Vol. 38, No. 1, pp. 61-63.

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25. Serot et al., (September 1992), "Antibodies to choroids plexus in senile dementia of Alzheimer's type" *J Clin Pathol*, Vol. 45, No. 9, pp. 781-783. (Abstract).
26. Singh et al., (1989) "Increase of immunoglobulin G3 subclass is related to brain autoantibody in Alzheimer's disease but not in Down's syndrome", *Autoimmunity*, Vol. 3, No. 2, pp. 95-101. (Abstract).
27. Kumar et al., (1988) "Serum IgG brain reactive antibodies in Alzheimer disease and Down syndrome", *Alzheimer Dis. Assoc. Disord*, Vol. 2, No. 1, pp. 50-55. (Abstract). \*
28. Franseschi et al., (July 1989), "Neuron-binding antibodies in Alzheimer's Disease and Down's syndrome", *J. Gerontol*, Vol., 44, No. 4, pp. 128-30. (Abstract).
29. Mecocci et al., (September 1992), "Serum autoantibodies against glial fibrillary acidic protein in brain aging and senile dementias" *Brain Behav Immun*, Vol. 6, No. 3, pp. 286-92. (Abstract).
30. Heinonen et al., (January 1993), "Circulating immune complexes in sera from patients with Alzheimer's disease, multi-infaract dementia and Down's syndrome", *Neurosci Lett*, Vol. 149, No. 1, pp. 67-70. (Abstract).
31. Ryskova et al., (1998), "Serum antibodies against brain tissue in patients with multiple sclerosis", *Sb Ved Pr Lek Fak Karlovy University HNradcy Kralove Supl.*, Vol. 31, No. 4, pp. 407-11. (Abstract). \*
32. Henneberg et al., (November 1991), "Antibodies to brain tissue in sera of patients with chronic progressive multiple sclerosis", *J Neuroimmunol*, Vol. 34, No. 2-3, pp. 223-27. (Abstract).
33. Hassin-Baer et al., (March 1992), "Antibodies from Down's syndrome patients bind to the same cholinergin neurofilament protein recognized by Alzheimer's disease antibodies", *Neurology*, Vol. 42, No. 3, pp. 551-55. (Abstract).
34. Vazquez et al., (August 1996), "Antibodies to human brain spectrin in Alzheimer's disease." *J Neuroimmunol*, vol. 68, No. 1-2, pp. 39-144. (Abstract).
35. Fillit et al., (March 1987, "Antivascular antibodies in the sera of patients with senile demential of the Alzheimer's type", *J Gerontol*, Vol. 42, No. 2, pp. 182-184 (Abstract).

36. David M. Wilson et al., "Free fatty acids stimulate the polymerization of tau and amyloid beta peptides: In vitro evidence for a common effector of pathogenesis in Alzheimer's disease", *American Journal of Pathology*, Vol. 150, No. 6, (1997), pages 2181-2195. XP000952986.
37. Shi Du Yan et al., "Non-enzymatically glycosylated tau in Alzheimer's disease induces neuronal oxidant stress resulting in cytokine gene expression and release of amyloid-beta-peptide", *Nature Medicine*, (1995) 1/7, (693-699). XP002151418.
38. Mark P. Mattson et al., "4-Hydroxynonenal, a product of lipid peroxidation, inhibits dephosphorylation of the microtubule-associated protein tau", *Neuroreport*, Vol. 8, No. 9-10, 1997, pages 2275-2281. XP000953016.
39. Data Base Biosis 'Online! Biosciences Information Service, Philadelphia, PA, US; 1990, Ksiezak-Reding et al., "Mapping of the ALZ 50 Epitope in Microtubule-Associated Proteins Taus", Database accession no. PREV199089120028, XP002151419.

Also, enclosed is a copy of the International Search Report in which the above-listed references were cited during the prosecution of a corresponding PCT application.

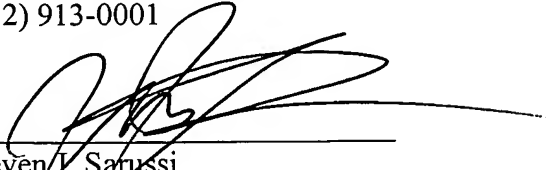
In accordance with MPEP Sections 609 and 707.05(b), it is requested the document cited (including any cited in applicant's specification which is not repeated on the attached Form PTO-1449) be given thorough consideration and that it be cited of record in the prosecution history of the present application by initialing on Form PTO-1449. Such initialing is requested even if the Examiner does not consider a cited document to be sufficiently pertinent to use in a rejection, or otherwise does not consider it to be prior art for any reason, or even if the Examiner does not

believe that the guidelines for citation have been fully complied with. This is requested so that each document becomes listed on the face of the patent issuing on the present application

Respectfully submitted  
McDONNELL BOEHNEN  
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Dated: April 13, 2004

By:

  
Steven J. Samussi  
Reg. No. 32,784

Form PTO-1449 (modified)

Atty. Docket No.  
98-614-DSerial No.  
10/017,822

List of Patents and Publications for Applicant's

## INFORMATION DISCLOSURE STATEMENT

(Use several sheets if necessary)

Applicant

DeBarnardis et al.

Filing Date:  
December 12, 2001Group:  
1647

## U.S. Patent Documents

Exam. Init.	Ref. Des.	Document Number	Date	Name	Class	Sub Class	Filing Date of App.
	A1	5,492,812	02/20/96	Vooheis et al.			11/30/93
	A2	5,342,580	08/30/94	Brenner			04/17/90

## Foreign Patent Documents

Exam. Init.	Ref. Des.	Document Number	Date	Country	Class	Sub Class	Translation Yes/No
	B1	WO 96 20218	07/4/96	PCT			
	B2	EP 0 909 814	04/21/99	EP			
	B3						
	B4						
	B5						

## Other Art (Including Author, Title, Date Pertinent Pages, Etc.)

Exam. Init.	Ref. Des.	Citation
	C1	Foley et al., (1988), "Evidence for the presence of antibodies to cholinergic neurons in the serum of patients with Alzheimer's disease", <i>Journal of Neurology</i> , Vol. 235, pp. 466-471.
	C2	Gaskin, "Human Antibodies to Alzheimer's Disease and Normal Neural Elements", <i>Antibodies to Alzheimer's Disease</i> , pp 137-145.
	C3	Gaskin et al., (January 1987), "Autoantibodies To Neurofibrillary Tangles and Brain Tissue in Alzheimer's Disease: Establishment of Epstein-Barr Virus-transformed Antibody-producing Cell Lines", <i>J. Exp. Med.</i> , Vol. 165, pp. 245-250.
	C4	Lopez et al., (August 1992), "Serum Autoantibodies in Patients With Alzheimer's Disease and Vascular Dementia and in Nondemented Control Subjects", <i>Stroke</i> , Vol. 23, No. 8, pp. 1078-1083.
	C5	McRae et al., (August 1993), "Cerebrospinal fluid microglial antibodies: potential diagnostic markers for immune mechanisms in Alzheimer's disease", <i>Behavioural Brain Research</i> , Vol. 57, pp. 225-234.
	C6	Mecocci et al., (1993), "Antihistone and Anti-dsDNA Autoantibodies in Alzheimer's Disease and Vascular Dementia", <i>Society of Biological Psychiatry</i> , Vol. 33, pp. 380-385.

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	C7	Mecocci et al., (1995), "Serum anti-GFAP and anti-S100 autoantibodies in brain aging, Alzheimer's disease and vascular dementia", <i>Journal of Neuroimmunology</i> , Vol. 57, pp. 165-170.
	C8	Singh et al., (1992), "Immunoblot detection of antibodies to myelin basic protein in Alzheimer's disease patients", <i>Neuroscience Letters</i> , Vol. 147, pp. 25-28.
	C9	Singh et al., (1986), "Detection of Brain Autoantibodies in the serum of patients with Alzheimer's disease but not Down's Syndrome", <i>Immunology Letters</i> , Vol. 12, pp. 277-280.
	C10	Tanaka et al., (1989), "Enzyme-linked immunosorbent assay for human autoantibody to glial fibrillary acidic protein: higher titer of the antibody is detected in serum of patients with Alzheimer's disease", <i>Acta Neurol. Scand.</i> , Vol. 80, pp. 554-560.
	C11	Tchernakov et al., (1992), "Alzheimer's disease and Down's syndrome antibodies bind to the heavy neurofilament protein of cholinergic neurons", <i>Immunological Factors in Alzheimer's Disease</i> , pp. 670-675.
	C12	Schott et al. (January 31, 1996), "Autoantibody reactivity in serum of patients with Alzheimer' disease and other age related dementia", <i>Psychiatry Res.</i> , Vol. 50, No. 3, pp. 251-54. (Abstract).
	C13	Lopez et al., (November 1991), "Serum auto-antibodies in Alzheimer's disease" <i>Acta Neural Scand</i> , Vol. 84, No. 5, pp. 441-44. (Abstract).
	C14	Ounanian et al., (1990), "Antibodies to viral antigens, xenoantigens and autoantigens in Alzheimer's disease". <i>J Clin Lab Anal</i> , Vol. 4, No. 5, pp. 367-75. (Abstract).
	C15	Loeffler et al, (February 1997), "Immunocytochemical detection of anti-hippocampal antibodies in Alzheimer's disease and normal cerebrospinal fluid", <i>Neurochem Res.</i> , Vol. 22, No. 2 pp. 209-14. (Abstract).
	C16	McRae et al., (May-August 1996), "Microglial Cerebrospinal fluid antibodies. Significance for Alzheimer disease", <i>Mol. Chem. Neuropathol</i> , Vol. 28, No. 1-3, pp. 89-95. (Abstract).
	C17	Dahlstrom et al., (August-December 1994), "Alzheimer's disease cerebrospinal fluid antibodies display selectivity for Microglia. Investigations with cell cultures and human cortical biopsies" <i>Mol Neurobiol</i> , Vol. 9, No. 1-3, pp. 41-54. (Abstract).
	C18	Dahlstrom et al., (1990), "8investigations on auto-antibodies in Alzheimer's and Parkinson's disease, using defined neuronal cultures" <i>J Neural Transm Suppl.</i> , Vol. 29, 195-206. (Abstract).
	C19	Sugiura et al., (January 1989), "Detection of anti-cerebral autoantibodies in schizophrenia and Alzheimer's disease" <i>J Clin lab Immunol</i> , Vol. 28, No. 1, pp. 1-3. (Abstract).

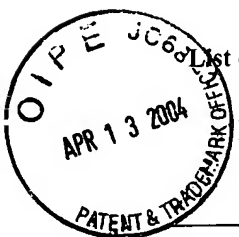
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	C20	Bahmanyar et al., (October 1983), "Serum antibodies to neurofilament antigens in patients with neurological and other diseases and in healthy controls", <i>J Neuroimmunol</i> , Vol. 5, No. 2, pp. 191-196. (Abstract).
	C21	Genovesi et al., (March 1996), "Relationship between autoimmune thyroid disease and Alzheimer's disease", <i>Panminerva Med.</i> , Vol. 38, No. 1, pp. 61-63. (Abstract). ✓
	C22	Serot et al., (September 1992), "Antibodies to choroids plexus in senile dementia of Alzheimer's type" <i>J Clin Pathol</i> , Vol. 45, No. 9, pp. 781-783. (Abstract).
	C23	Singh et al., (1989) "Increase of immunoglobulin G3 subclass is related to brain autoantibody in Alzheimer's disease but not in Down's syndrome", <i>Autoimmunity</i> , Vol. 3, No. 2, pp. 95-101. (Abstract).
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	C25	Franceschi et al., (July 1989), "Neuron-binding antibodies in Alzheimer's Disease and Down's syndrome", <i>J. Gerontol</i> , Vol., 44, No. 4, pp. 128-30. (Abstract).
	C26	Mecocci et al., (September 1992), "Serum autoantibodies against glial fibrillary acidic protein in brain aging and senile dementias" <i>Brain Behav Immun</i> , Vol. 6, No. 3, pp. 286-92. (Abstract).
	C27	Heinonen et al., (January 1993), "Circulating immune complexes in sera from patients with Alzheimer's disease, multi-infarct dementia and Down's syndrome", <i>Neurosci Lett</i> , Vol. 149, No. 1, pp. 67-70. (Abstract).
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	C30	Hassin-Baer et al., (March 1992), "Antibodies from Down's syndrome patients bind to the same cholinergic neurofilament protein recognized by Alzheimer's disease antibodies", <i>Neurology</i> , Vol. 42, No. 3, pp. 551-55. (Abstract).
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	C34	Shi Du Yan et al., "Non-enzymatically glycosylated tau in Alzheimer's disease induces neuronal oxidant stress resulting in cytokine gene expression and release of amyloid beta-peptide", <i>Nature Medicine</i> , (1995) 1/7, (693-699). XP002151418.
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